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論文題目	Characteristics and perioperative changes of nutritional parameters in patients undergoing living donor liver transplantation （生体肝移植患者における栄養学的パラメーターの特徴と周術期変化に関する検討）		

（論文内容の要旨）

Summary

Background: Protein-energy malnutrition and perioperative derangements of various serum biochemical nutritional and related metabolic parameters are common in patients with end-stage liver disease requiring liver transplantation (LT).

The aim of the study was to examine the characteristics of pre-transplant nutritional status and the impact of pre-admission administration of branched-chain amino- acids (BCAA) treatment on pre-transplant skeletal muscle mass, nutritional and related metabolic parameters' levels and on post-transplant outcomes. The benefit of LT was also explained with respect to each parameter's changes and examined the impact of graft weight to recipient body weight ratio (GRWR) on such changes.

Methodology: Preoperative skeletal muscle mass, nutritional and the related metabolic parameters' levels were compared in 129 patients undergoing adult-to-adult living donor liver transplantation (LDLT) whether they received BCAA treatment before admission or not. The relationships among these parameters and the risk factors for post-transplant bacteremia and early mortality after LT were all examined focusing on nutritional parameters. Each parameter's course was investigated in 208 adult recipients for one year after LDLT and sub-analyzed perioperative changes in the parameters using a GRWR of 0.8% as the cutoff point.

Results: Marked decreases in zinc, prealbumin, and total lymphocyte count and marked increases in ammonia and tyrosine were seen before LDLT. Prealbumin and BCAA-to-tyrosine ratio (BTR) were significantly higher while tyrosine was lower in BCAA-pre-supplemented group than non-pre-supplemented group, while skeletal muscle mass, total lymphocyte count, zinc, BCAA and ammonia levels were not significantly different.

Multivariate predictors of post-transplant bacteremia were: Child-Pugh class C (P=0.012), low preoperative total lymphocyte count (P=0.027), operative blood loss ≥ 10 L (P=0.039) and absence of pre-admission BCAA treatment (P=0.040). Nutritional/metabolic parameters and pre-admission BCAA treatment were not crucial for post-transplant early mortality.

Liver disease-induced high pre-transplant ammonia, tyrosine, low BTR and zinc normalized within two weeks after transplantation, and total lymphocyte count normalized in two months, while low pre-transplant prealbumin took one year to normalize. BCAA, zinc and total lymphocyte count transiently dropped shortly after transplantation, then corrected later on. An accelerated recovery of ammonia and tyrosine levels and the BTR was found with larger-sized grafts, especially early after transplantation, while, zinc, prealbumin, BCAA and total lymphocyte count recovered irrespective of graft size.

Conclusion: Pre-admission BCAA therapy could ameliorate preoperative amino acid imbalance and the incidence of post-transplant bacteremia. Graft size had little impact on the recovery of nutritional/metabolic parameters except ammonia and tyrosine levels.

（論文審査の結果の要旨）

肝移植患者の多くは蛋白エネルギー低栄養を伴うが、周術期変動や術前分岐鎖アミノ酸（BCAA）投与の効果は明らかではない。今回申請者は、当科成人肝移植症例において、術前栄養代謝パラメーター、入院前分岐鎖アミノ酸投与の効果、術後死亡ならびに菌血症発症危険因子、さらに栄養代謝パラメーターの周術期変動と移植片の大きさの影響などを検討した。

肝移植前、亜鉛やアンモニア、総リンパ球数は著明に低下し、一方、アンモニアやチロシンは著明に上昇していた。入院前 BCAA 投与群は非投与群に比べ、有意にプレアルブミンや BCAA-チロシン比が上昇し、チロシンが低下していた。多変量解析にて、Child-Pugh C 肝硬変、術前低総リンパ球数、大量出血、入院前 BCAA 非投与が移植後菌血症発症の独立危険因子であった。

肝移植後、アンモニアやチロシン、亜鉛などは早期に正常値に回復したが、プレアルブミンは回復に 1 年を要した。アンモニアやチロシンなどの回復は大きな移植片の症例で早期に回復した。一方、亜鉛やプレアルブミン、BCAA、総リンパ球数の回復は移植片の大きさの影響は受けなかった。

以上の結果から、入院前 BCAA 投与は術前アミノ酸インバランスを改善させ、移植後菌血症の発症を抑制すること、および栄養代謝パラメーターの周術期変動が明らかになり、肝移植周術期栄養療法の確立に寄与すると考えられた。

以上の研究は肝移植術前 BCAA 投与の効果や周術期栄養代謝パラメーターの変動の解明に貢献し、肝移植周術期栄養療法の確立や予後改善に寄与するところが多い。

したがって、本論文は博士（医学）の学位論文として価値あるものと認める。

なお、本学位授与申請者は、平成 28 年 12 月 9 日実施の論文内容とそれに関連した試問を受け、合格と認められたものである。